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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/202,181	12/10/98	REISNER	Y	REISNER=5

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EXAMINER	
ZEMAN, R	
ART UNIT	**PAPER NUMBER**
1645	5

DATE MAILED: 03/29/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/202,181	Reisner et al.
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Dec 10, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-18* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-18* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ Sequence Letter

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Specification

The use of the trademarks Engerix-B™, Stat View II, Microsoft Excel®, and Tween has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Additionally, the text is unreadable on page 4 line 6, page 9 line 23 and page 10 line 15. Appropriate corrections are required.

Abbreviations such as "Ad antigen" , "HB", and "o.n." (see page 12) are used throughout the specification without disclosing what the abbreviations stand for. Appropriate corrections are required.

This application contains sequence disclosures (see figures 10 and 11) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Any questions regarding compliance with the sequence rules requirements

specifically should be directed to the departments listed at the bottom of the Notice to Comply. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that hybridoma cell lines that secrete the monoclonal antibodies 18.5.1013 and 19.75.5 are required in order to practice the claimed invention. Specifically, it is noted that claims 5-8 recite deposited material in the body of the claim and that claims 9-18 depend from claims reciting the deposited material. The deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention {see 37 CFR 1.808(a)}. The Examiner acknowledges the deposit of organisms under European Collection of Cell Cultures (ECACC) under Accession No. 96052170 and 96052168, respectively, in partial compliance with this requirement. However, the deposits are not in full compliance with 37 CFR 1.803-1.809.

If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, than an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository *and that* the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

3) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

Claims 9, 11 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of HBV infection, does not reasonably provide enablement for prevention of HBV infection. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The above rejected claims are drawn to prophylactic antibody vaccine compositions. To be a prophylactic vaccine, the vaccine must provide protective immunity, demonstrable by viral challenge experiments, in a reasonable model system. The specification, as filed, does not set forth that the claimed composition provides any sort of protective immunity in any model system which can be extrapolated to humans or higher mammals. Applicant describes a "combined prophylaxis/inhibition mode" wherein a mouse was treated with antibody 19.79.5 before transplantation of human liver fragments infected with HBV *ex vivo* in the presence of antibody 19.79.5. Applicant further discloses that there was merely a reduction in the number of infected animals (see page 35, second paragraph). Additionally, Applicant describes a "combined inhibition/treatment mode" wherein HBV positive human serum was preincubated with antibody 19.79.5 followed by *ex vivo* liver infection; mice were treated with antibody 19.79.5 at days 0 and 7 post transplantation. Again, no protective immunity was demonstrated as there was merely a reduction in the number

of infected animals not a prevention of HBV infection. Moreover, Applicant discloses that reduction in the number of infected animals was dependent on continued antibody treatment since all animals became infected two weeks after the cessation of antibody treatment (see page 35, lines 16-18). While the skill in the art of virology is high, to date, prediction of protective immunity for any given composition is quite unpredictable. Given the lack of success in the art, the lack of working examples, and the unpredictability of the generation of protective immunity, the specification, as filed, is not enabling for such vaccines.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 9-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 and 12 are rendered vague and indefinite by the confusing way they are recited and the improper punctuation used. For example, in claim 1, the phrase "...immunizing a chimeric rodent M4 having xenogenic hematopoietic cells with Hepatitis B surface antigen HBVsAg such that....." is confusing. Do the xenogenic hematopoietic cells have the HBVsAg or is the HBVsAg what is used to immunize the chimeric rodent M4? Additionally, it is unclear what is meant by the term "removing". How are the cells removed? From where? Claim 12 is

equally confusing in step (b). As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 4 contains the trademark/trade name Engerix-B™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a Hepatitis B surface antigen and, accordingly, the identification/description is indefinite.

Claim 5 is rejected as it recites improper Markush language, rendering the claim indefinite. Proper language for claim 5 would be "....selected from the from the group consisting of (a) the monoclonal antibody 18.5.1013 which is secreted by the hybridoma cell line deposited in the European Collection of Cell Cultures (ECACC) under Accession No. 96052170 **and** (b) fragments of (a) which....."

Claim 6 is rejected as it recites improper Markush language, rendering the claim indefinite. Proper language for claim 6 would be "....selected from the from the group consisting of (a) the monoclonal antibody 19.79.5 which is secreted by the hybridoma cell line deposited in

the European Collection of Cell Cultures (ECACC) under Accession No. 96052168 **and** (b) fragments of (a) which....."

Claims 5 and 6 are rendered vague and indefinite by the use of the phrase "substantially retains the binding characteristics of the whole antibody". Applicant fails to delineate what binding characteristics apply or what is meant by "substantially". Must the fragment be able to bind all epitopes that the whole antibody can with the same affinity? Can the affinities be different? If so to what degree? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claims 10, 11, 13 and 14 are rendered vague and indefinite by the use of the terms "according to claim 5" and "in accordance with claim 5". These terms imply that claim 5 recites method steps for the administration of the claimed antibodies to an individual. Claim 5 recites no such method steps. Consequently it is impossible to determine the metes and bounds of the claimed invention.

Claims 10 and 17 are rendered vague and indefinite by the use of the term "therapeutically effective amount". It is unclear what Applicant is claiming. What threshold must be achieved in order to be deemed "effective"? How is efficacy measured? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 12 is rendered vague and indefinite by the use of the phrase "antibody of any of Claim 5". It is impossible to determine the metes and bounds of the claimed invention. Use of the phrase "antibody of claim 5" is suggested.

Claims 13, 14 and 18 provide for the use of an antibody, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 13, 14 and 18 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 17 is rendered vague and indefinite by the use of the phrase "composition according to any one of claims 9". It is impossible to determine the metes and bounds of the claimed invention. Use of the phrase "composition according to claim 9" is suggested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marcus et al. (Blood, Vol 86, No. 1 July 1, 1995 pages 398-406; IDS-2) in view of Ichimori et al. (Biochemical and Biophysical Research Communications. Vol. 142, No. 3. Feb. 13, 1987 pages 805-812; IDS-2).

Claims 1-4 are being interpreted as being drawn to a process for obtaining human monoclonal antibodies (hMoAB) capable of binding to Hepatitis B virus surface antigen (HBVsAg) comprising:

1. irradiating a Balb/c mouse as to destroy its hemapoietic cells;

2. transplanting hemapoietic cells from a SCID mouse;

3. injecting said Balb/c mouse with PBMCs from humans with high titers of anti-HBVsAg; antibodies

4. isolating and immortalizing the antibody producing cells;

5. selecting and cloning the immortalized antibody producing cells that secrete antibodies capable of binding HBVsAg; and

6. isolating the antibodies produced by said cells.

Marcus et al. disclose methods that enable the generation of human/mouse chimera by adoptive transfer of human peripheral blood mononuclear cells (PBMC) into lethally irradiated Balb/c mice, radioprotected with the hemapoietic cells (bone marrow) from SCID mice. Marcus et al. further disclose that such mouse/human chimera demonstrate a marked humoral response to recall antigens like hepatitis B surface antigen (see pages 398-399). Marcus et al., differs from the claimed invention in that the antibodies produced by said methods are polyclonal. Consequently, they do not disclose methods for the immortalization or cloning of the cells that produce a monoclonal HBVsAg antibody. Marcus et al. do suggest that their human/mouse chimera would be useful for the generation of fusion partners for monoclonal antibody production (see page 405, second paragraph).

Ichimori et al. disclose the methods for establishing hybridomas secreting monoclonal antibody against HBVsAg. Ichimori et al. transformed PBMCs from human donors with high anti-HBVsAg antibody titers and fused them with a human B lymphoblastoid cells (see page 806). The resulting hybridomas were cloned and tested by EIA for anti-HBVsAg antibody production (see page 807).

In view of the above disclosures, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention to have used the methods of Ichimori et al. to immortalize, clone, and isolate the anti-HBVsAg producing chimera of Marcus et al.(i.e. establish a hybridoma) as suggested by Marcus et al.

Conclusion

No claim is allowed

Claims 5-18 have been found to be free of the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Anthony Caputa, can be reached at (703)308-3995.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman

March 24, 2000

Application No.:09/202181

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s)

[X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

[X] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

[X] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

[ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

[ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

[ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

[ ] 7. Other: _____

Applicant Must Provide:

[X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

[X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

[X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR RESPONSE